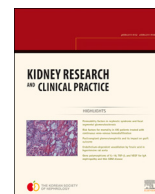




# Kidney Research and Clinical Practice

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## Letter and Reply

## The use of tacrolimus in the management of minimal change disease



### To the Editor:

Kim et al [1] showed interesting results that tacrolimus and low-dose prednisolone therapy induced complete remission rapidly and effectively in adult patients with minimal change disease (MCD). MCD has been regarded as an immunological disorder. Recent works, however, have dramatically enhanced the understanding of podocyte biology, which may be the mainstay involved in the pathogenesis of MCD, and many treatment options that were thought to work via immunosuppressive pathways are now known to have a direct nonimmunological effect on the podocyte [2]. Calcineurin inhibitors are frequently used to treat relapsing or resistant nephrotic syndrome [3]. There are several issues to be resolved, however, before taking tacrolimus as first-line therapy in adults with MCD.

Despite its recognized efficacy, there are still limited data on the renal histological changes that occur with tacrolimus therapy. Histological nephrotoxicity of tacrolimus has been well established in patients with nephrotic syndrome [4]. Previous studies suggested the lowest possible dose of tacrolimus be used in children with steroid-dependent or steroid-resistant nephrotic syndrome [5]. Kim et al treated patients with 0.05 mg/kg of tacrolimus as a fixed dose. Only one patient was treated with a lower dosage. The optimal dose of tacrolimus for inducing complete remission of adult MCD is the first question to be answered. There would be individual differences in the trough level of tacrolimus because of pharmacogenomics. To prevent toxicity, dose adjustment is necessary according to the trough level of tacrolimus [5].

Kim et al treated patients with 0.05 mg/kg of tacrolimus for 16 weeks. It is necessary to establish the ideal duration of tacrolimus therapy for the treatment protocol, addressing when its tapering begins. It is currently unknown whether complete discontinuance of all immunosuppressants is preferable to their long-term continuation at a low dosage. The ideal length of tacrolimus therapy is the second question to be answered [6].

Although this pilot trial included a small number of patients over a short period of time, tacrolimus produced a reliable, beneficial effect in adults with steroid-resistant or steroid-dependent MCD. Further investigations on a larger number of patients over longer follow-up periods are required to evaluate the clinical efficacy and effectiveness (including relapse rates and side effects) of tacrolimus in adult patients with MCD.

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### In Reply:

Thank you for your interest in our manuscript. First of all, the tacrolimus was not stopped after remission but the dosage was tapered down over various time-periods. As you mentioned, the adequate dosage and duration of tacrolimus for the treatment of minimal change lesion (MCD) are still being debated. We checked the trough level of tacrolimus during our study to monitor the toxicity as a protocol and got a mean level of  $5.99 \pm 2.63$  (0.3–12.3) ng/mL, which was variable from patient to patient. The higher trough level did not give a guarantee of remission, and patients with a lower trough level also effectively achieved remission. In a small, open, prospective cohort study with tacrolimus for MCD patients, the authors maintained low-dose prednisolone (0.5 mg/kg/day)

and tacrolimus (0.05 mg/kg/day) for 24 weeks and followed patients for 23.0 months after cessation of tacrolimus [1]. During the observation period after the discontinuation of tacrolimus, 50% of patients (6/12 patients) remained in remission.

In this study, we did not plan to show the efficacy of tacrolimus to maintain remission in MCD and used a fixed dose of this drug. We cannot therefore suggest an appropriate schedule of tacrolimus for use in patients with MCD. We need well-designed clinical studies in the near future to determine the verified duration and dosage of tacrolimus to treat MCD.

#### **Conflict of interest**

None to declare.

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#### **Reference**

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